



## General

### Guideline Title

Congress of Neurological Surgeons systematic review and evidence-based guidelines on emerging therapies for the treatment of patients with vestibular schwannomas.

### Bibliographic Source(s)

Van Gompel JJ, Agazzi S, Carlson ML, Adewumi DA, Hadjipanayis CG, Uhm JH, Olson JJ. Congress of Neurological Surgeons systematic review and evidence-based guidelines on emerging therapies for the treatment of patients with vestibular schwannomas. *Neurosurgery*. 2018 Feb 1;82(2):E52-4. [PubMed](#)

### Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report [Clinical Practice Guidelines We Can Trust](#).

■■■■■= Poor ■■■■■= Fair ■■■■■= Good ■■■■■= Very Good ■■■■■= Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source
■■■■■	Disclosure and Management of Financial Conflict of Interests
	Guideline Development Group Composition
YES	Multidisciplinary Group
UNKNOWN	Methodologist Involvement

	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
	Search Strategy
	Study Selection
	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
	Grading the Quality or Strength of Evidence
	Benefits and Harms of Recommendations
	Evidence Summary Supporting Recommendations
	Rating the Strength of Recommendations
	Specific and Unambiguous Articulation of Recommendations
	External Review
	Updating

## Recommendations

### Major Recommendations

Definitions for the classification of evidence (I-III) and levels of recommendations (1-3) are provided at the end of the "Major Recommendations" field.

#### Medical Therapy

#### Question

What is the role of bevacizumab in the treatment of patients with vestibular schwannomas (VSs)?

#### Target Population

Adults with histologically proven or suspected vestibular schwannomas with neurofibromatosis type 2 (NF2).

#### Recommendations

*Level 3:* It is recommended that bevacizumab be administered in order to radiographically reduce the size or prolong tumor stability in patients with NF2 without surgical options.

*Level 3:* It is recommended that bevacizumab be administered to improve hearing or prolong time to hearing loss in patients with NF2 without surgical options.

#### Question

Is there a role for lapatinib, erlotinib, or everolimus in the treatment of patients with vestibular schwannomas?

#### Target Population

Adults with histologically proven or suspected VSs and NF2

#### Recommendations

*Level 3:* Lapatinib may be considered for use in reducing vestibular schwannoma size and improvement in hearing in NF2.

*Level 3:* Erlotinib is not recommended for use in reducing vestibular schwannoma size or improvement in hearing in patients with NF2.

*Level 3:* Everolimus is not recommended for use in reducing vestibular schwannoma size or improvement in hearing in NF2.

#### Question

What is the role of aspirin, to augment inflammatory response, in the treatment of patients with vestibular schwannomas?

#### Target Population

Any patient with a vestibular schwannoma undergoing observation.

#### Recommendation

*Level 3:* It is recommended that aspirin administration may be considered for use in patients undergoing observation of their vestibular schwannomas.

#### Question

Is there a role for treatment of vasospasm, i.e., nimodipine or hydroxyethyl starch, perioperatively to improve facial nerve outcomes in patients with vestibular schwannomas?

#### Target Population

Adults with histologically proven or suspected vestibular schwannomas.

#### Recommendation

*Level 3:* Perioperative treatment with nimodipine (or with the addition of hydroxyethyl starch) should be considered to improve postoperative facial nerve outcomes and may improve hearing outcomes.

#### Prehabilitation

#### Question

Is there a role for preoperative vestibular rehab or vestibular ablation with gentamicin for patients surgically treated for vestibular schwannomas?

#### Target Population

Adults with histologically proven or suspected vestibular schwannomas.

#### Recommendations

*Level 3:* Preoperative vestibular rehabilitation is recommended to aid in postoperative mobility after vestibular schwannoma surgery.

*Level 3:* Preoperative gentamicin ablation of the vestibular apparatus should be considered to improve postoperative mobility after vestibular schwannoma surgery.

## Surgical Therapy

### Question

Does endoscopic assistance make a difference in resection or outcomes in patients with vestibular schwannomas?

### Target Population

Vestibular schwannoma patients, who are surgical candidates. Inclusion in this analysis required resection utilizing the endoscope, either as the primary operative visualization or microscopic assistance with more than 20 patients treated.

### Recommendation

*Level 3:* Endoscopic assistance is a surgical technique that the surgeon may choose to use in order to aid in visualization.

### Definitions

American Association of Neurological Surgeons/Congress of Neurological Surgeons Classification of Evidence on Therapeutic Effectiveness

Evidence Classification	
Class I Evidence	Evidence provided by one or more well-designed randomized controlled clinical trials, including overview (meta-analyses) of such trials
Class II Evidence	Evidence provided by well-designed observational studies with concurrent controls (e.g., case-control and cohort studies)
Class III Evidence	Evidence provided by expert opinion, case series, case reports, and studies with historical controls

American Association of Neurological Surgeons/Congress of Neurological Surgeons Levels of Recommendation

Levels of Recommendation	
Level 1	Generally accepted principles for patient management, which reflect a high degree of clinical certainty (usually this requires class I evidence which directly addresses the clinical questions or overwhelming class II evidence when circumstances preclude randomized clinical trials)
Level 2	Recommendations for patient management which reflect clinical certainty (usually this requires class II evidence or a strong consensus of class III evidence)
Level 3	Other strategies for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion)

## Clinical Algorithm(s)

None provided

## Scope

## Disease/Condition(s)

Vestibular schwannomas

# Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

## Clinical Specialty

Neurological Surgery

Neurology

Oncology

Otolaryngology

## Intended Users

Physicians

## Guideline Objective(s)

To assess both comparative and noncomparative studies of emerging therapies for vestibular schwannomas (VSs)

## Target Population

- Adults with histologically proven or suspected vestibular schwannomas (VSs)
- Adults with VSs with neurofibromatosis type 2 (NF2)

## Interventions and Practices Considered

1. Medical therapy
  - Bevacizumab
  - Lapatinib
  - Aspirin
  - Nimodipine
2. Prehabilitation
  - Preoperative vestibular rehabilitation
  - Preoperative gentamicin ablation of the vestibular apparatus
3. Surgical therapy: endoscopic assistance

Note: The following interventions were considered but not recommended: erlotinib, everolimus.

## Major Outcomes Considered

- Tumor size rates
- Hearing preservation rates
- Facial nerve function
- Vestibular function
- Tumor recurrence rates
- Adverse effects of treatment

# Methodology

## Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

### Search Strategies

The task force collaborated with a medical librarian to search for articles published between January 1, 1966 and December 31, 2014. Two electronic databases, PubMed and the Cochrane Central Register of Controlled Trials, were searched. Strategies for searching electronic databases were constructed by the evidence-based clinical practice guideline taskforce members and the medical librarian using previously published search strategies to identify relevant studies.

The task force supplemented searches of electronic databases with manual screening of the bibliographies of all retrieved publications. The task force also searched the bibliographies of recent systematic reviews and other review articles for potentially relevant citations. All articles identified were subject to the study selection criteria listed below.

The task force made every effort to obtain a complete set of relevant articles to ensure the guideline is not based on a biased subset of articles. The specific search strategies for each question can be found in the full guideline (see the "Availability of Companion Documents" field).

### Article Inclusion/Exclusion Criteria

Seventy-eight citations were manually reviewed by the team with specific inclusion and exclusion criteria as outlined below. Two independent reviewers reviewed and abstracted full-text data for each article, and the 2 sets of data were compared for agreement by a third party. Inconsistencies were re-reviewed, and disagreements were resolved by consensus. Only citations that considered adult patients focusing on surgical treatment of vestibular schwannomas (VSs) were considered. To be included in this guideline, an article has to be a report of a study that:

- Investigated patients suspected of having VSs

- Patients  $\geq 18$  years of age

- Was in humans

- Published between January 1, 1966 and December 31, 2014

- Quantitatively presented results

- Was not an in vitro study (for novel molecular markers, in vitro studies were included on patient samples)

- Was not a biomechanical study

- Was not performed on cadavers

- Was published in English

- Was not a meeting abstract, editorial, letter, or commentary

- Studies may include mixed pathology; however, the data pertaining to VSs were abstractable from the paper.

- >5 patients or patient samples

The task force did not include systematic reviews, guidelines, or meta-analyses conducted by others. These documents are developed using different inclusion criteria than those specified in this guideline. Therefore, they may include studies that do not meet the inclusion criteria used for this guideline. The

task force recalled these documents if their abstract suggested that they might address one of the recommendations, and the bibliographies were searched for additional studies.

## Number of Source Documents

Twenty-two studies were included as evidence. See Figure 1 in the full guideline (see the "Availability of Companion Documents" field).

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

American Association of Neurological Surgeons/Congress of Neurological Surgeons Classification of Evidence on Therapeutic Effectiveness

Evidence Classification	
Class I Evidence	Evidence provided by one or more well-designed randomized controlled clinical trials, including overview (meta-analyses) of such trials
Class II Evidence	Evidence provided by well-designed observational studies with concurrent controls (e.g., case-control and cohort studies)
Class III Evidence	Evidence provided by expert opinion, case series, case reports, and studies with historical controls

## Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

Study Selection, Quality Assessment, and Statistical Methods

Articles that met the eligibility criteria were grouped according to the questions they addressed and used to create the evidence tables and scientific foundation sections. Reasons for exclusion for papers were also documented to be able to discuss pertinent problem citations in the scientific foundation as needed.

Studies that met the eligibility criteria were subject to more detailed scrutiny and had their data extracted by 1 reviewer and the extracted information was checked by 1 or more other reviewers. Evidence and summary tables, reporting the extracted study information and evidence classification, were generated for all the included studies for each of the questions. Evidence tables were created with the most recent data first and subsequent listings in retrograde chronological order. The table headings consisted of first author name and year, followed by a brief study description, chosen data class, and conclusion. The authors were directed to craft the data in the tables in a succinct and fact-filled manner to allow for rapid understanding of the literature entry by the readership. The literature in the evidence tables was expanded upon in the Results section of each guideline article to emphasize important points supporting its classification and contribution to recommendations. The method by which this was accomplished is expanded upon in the Joint Guideline Committee (JGC) Guideline Development Methodology document (see the "Availability of Companion Documents" field). Internal drafts of the tables and manuscripts were developed by sharing them between writers electronically, by telephone, and in face-to-face meetings. Summary and conclusion statements were included for each section, with comments on key issues for future investigation being added where pertinent.

# Methods Used to Formulate the Recommendations

Expert Consensus (Nominal Group Technique)

## Description of Methods Used to Formulate the Recommendations

### Writing Group and Question Establishment

The evidence-based clinical practice guideline taskforce members and the Joint Tumor Section of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS) have prioritized an update of the guidelines for management of vestibular schwannomas (VSs). A series of writers were identified and screened for conflict of interest. This group in turn agreed on a set of questions addressing the topic at hand and conducted a systematic review of the literature relevant to the use of emerging therapies in patients with sporadic VSs. Additional details of the systematic review are provided below and within the introduction and methodology chapter of the original guideline document (see the "Availability of Companion Documents" field).

### Classification of Evidence and Guideline Formulation

The concept of linking evidence to recommendations has been further formalized by the American Medical Association (AMA) and many specialty societies, including AANS, CNS, and the American Academy of Neurology (AAN). This formalization involves the designation of specific relationships between the strength of evidence and the strength of recommendations to avoid ambiguity. In the paradigm for therapeutic maneuvers as used in this section, evidence is classified according to the scheme in the "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for the Strength of the Recommendations" fields). A basis for these guidelines can be viewed in the Joint Guidelines Committee methodology document (see the "Availability of Companion Documents" field).

### Guideline Panel Consensus

Multidisciplinary writing groups were created for each section based on author expertise to address each of the disciplines and particular areas of therapy selected for these clinical guidelines. Each group was involved with literature selection, creation and editing of the evidence tables, and scientific foundations for their specific section and discipline. Using this information, the writing groups then drafted the recommendations in answer to the questions formulated at the beginning of the process, culminating in the clinical practice guideline for their respective discipline. The draft guidelines were then circulated to the entire clinical guideline panel to allow for multidisciplinary feedback, discussion, and ultimately approval.

## Rating Scheme for the Strength of the Recommendations

American Association of Neurological Surgeons/Congress of Neurological Surgeons Levels of Recommendation

Levels of Recommendation	
Level 1	Generally accepted principles for patient management, which reflect a high degree of clinical certainty (usually this requires class I evidence which directly addresses the clinical questions or overwhelming class II evidence when circumstances preclude randomized clinical trials)
Level 2	Recommendations for patient management which reflect clinical certainty (usually this requires class II evidence or a strong consensus of class III evidence)
Level 3	Other strategies for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion)

## Cost Analysis



A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

Internal Peer Review

## Description of Method of Guideline Validation

### Approval Process

The completed evidence-based clinical practice guidelines for the management of vestibular schwannomas (VSs) were presented to the Joint Guideline Committee (JGC) of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS) for review. The reviewers for the JGC were vetted by *Neurosurgery* for suitability and expertise to serve as reviewers for the purposes of publication in that journal also. The final product was then approved and endorsed by the executive committees of both the AANS and CNS before publication in *Neurosurgery*.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

- Aspirin is associated with less risk of tumor progression, with an odds ratio of 0.5 and a confidence interval of 0.29-0.85. Therefore, aspirin use may be useful in patients with vestibular schwannomas (VSs) undergoing observation.
- Several studies provide preliminary results that prehab and preoperative gentamicin ablation of the vestibular apparatus may improve postoperative recovery; however, formal data regarding recovery are lacking.
- Prehab and preoperative gentamicin ablation may provide unique opportunities in improving postoperative mobility for patients undergoing VS surgery where they have preoperative vestibular function.
- The summary of evidence suggests that endoscopic use for VS surgery does not appear to worsen outcome or complications. In addition, endoscopic assistance may aid in the prevention of postoperative CSF leaks by directly visualizing them for repair.

### Potential Harms

Side effects of treatment, including intracerebral hemorrhage and cerebrospinal fluid (CSF) leaks

## Qualifying Statements

# Qualifying Statements

## Disclaimer of Liability

This clinical systematic review and evidence-based guideline was developed by a multidisciplinary physician volunteer task force and serves as an educational tool designed to provide an accurate review of the subject matter covered. These guidelines are disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a competent physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

# Implementation of the Guideline

## Description of Implementation Strategy

An implementation strategy was not provided.

## Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

## IOM Care Need

Getting Better

Living with Illness

## IOM Domain

Effectiveness

# Identifying Information and Availability

## Bibliographic Source(s)

Van Gompel JJ, Agazzi S, Carlson ML, Adewumi DA, Hadjipanayis CG, Uhm JH, Olson JJ. Congress of Neurological Surgeons systematic review and evidence-based guidelines on emerging therapies for the treatment of patients with vestibular schwannomas. *Neurosurgery*. 2018 Feb 1;82(2):E52-4. [PubMed](#)

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2018 Feb

## Guideline Developer(s)

Congress of Neurological Surgeons - Professional Association

## Source(s) of Funding

These evidence-based clinical practice guidelines were funded exclusively by the Congress of Neurological Surgeons, the Tumor Section of the Congress of Neurological Surgeons, and the American Association of Neurological Surgeons, which received no funding from outside commercial sources to support the development of this document.

## Guideline Committee

Vestibular Schwannoma Evidence-Based Practice Guideline Task Force

## Composition of Group That Authored the Guideline

*Task Force Members:* Jamie J. Van Gompel, MD, Department of Neurosurgery and Department of Otorhinolaryngology, Mayo Clinic, Rochester, Minnesota; Siviero Agazzi, MD, MBA, Department of Neurosurgery and Brain Repair, College of Medicine, University of South Florida, Tampa, Florida; Matthew L. Carlson, MD, Department of Neurosurgery and Department of Otorhinolaryngology, Mayo Clinic, Rochester, Minnesota; Dare A. Adewumi, MD, The Greater Houston Neurosurgery Center, The Woodlands, Texas; Constantinos G. Hadjipanayis, MD, PhD, Department of Neurosurgery, Mount Sinai Beth Israel, Icahn School of Medicine at Mount Sinai, New York, New York; Joon H. Uhm, MD, Department of Neurology and Department of Oncology, Mayo Clinic, Rochester, Minnesota; Jeffrey J. Olson, MD, Department of Neurosurgery, Emory University School of Medicine, Atlanta, Georgia

## Financial Disclosures/Conflicts of Interest

### Conflict of Interest

The Vestibular Schwannoma Guidelines Task Force members were required to report all possible conflicts of interest (COIs) prior to beginning work on the guideline, using the COI disclosure form of the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Joint Guidelines Committee, including potential COIs that are unrelated to the topic of the guideline. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination. The CNS Guidelines Committee and Guideline Task Force Chair are given latitude to approve nominations of Task Force members with possible conflicts and address this by restricting the writing and reviewing privileges of that person to topics unrelated to the possible COIs. The conflict of interest findings are provided in detail in the full-text introduction and methods manuscript (see the "Availability of Companion Documents" field).

## Guideline Endorser(s)

American Association of Neurological Surgeons - Medical Specialty Society

## Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Guideline Availability

Available from the [Neurosurgery Web site](#) .

## Availability of Companion Documents

The following are available:

Congress of Neurological Surgeons systematic review and evidence-based guidelines on emerging therapies for the treatment of patients with vestibular schwannomas. Full guideline. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2017 Dec 22. 35 p. Available from the [Congress of Neurological Surgeons \(CNS\) Web site](#) .

Congress of Neurological Surgeons systematic review and evidence-based guidelines on the treatment of adults with vestibular schwannomas: introduction and methods. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2017 Dec 22. 28 p. Available from the [CNS Web site](#) .

Olson JJ, Kalkanis SN, Ryken TC. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the treatment of adults with vestibular schwannomas: executive summary. Neurosurgery. 2018 Feb 1;82(2):129-34. Available from the [Neurosurgery Web site](#) .

Congress of Neurological Surgeons (CNS). Guideline development methodology: endorsed by the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), and the AANS/CNS Joint Guideline Committee. Schaumburg (IL): Congress of Neurological Surgeons (CNS); 2012 Feb. 12 p. Available from the [CNS Web site](#) .

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI Institute on May 7, 2018. The information was verified by the guideline developer on June 4, 2018.

This NEATS assessment was completed by ECRI Institute on April 25, 2018. The information was verified by the guideline developer on June 4, 2018.

## Copyright Statement

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